

### **REMARKS**

Claims 1, 3, 14, and 43-50 constitute the pending claims in the present application. The Office Action has acknowledged the full entry of the amendments filed on July 30, 2003. Applicants respectfully request reconsideration in view of the following remarks.

#### **Specification**

The Office Action asserts that the title of the invention is not descriptive, and requests Applicants to provide a new title that “is clearly indicative of the invention to which the claims are directed.”

Accordingly, Applicants have amended the title to obviate this objection. Applicants respectfully request reconsideration and withdrawal of the objection.

#### **Claim rejections under 35 USC §112, second paragraph**

Claims 1, 3, 14, 43-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office Action asserts that claim 1 recites “inhibit” rather than “inhibits.” Applicants have amended claim 1 to correct the grammatical error, thereby obviating the rejection to claim 1 and its dependent claims 3, 14, 43, 44, and 46-50.

The Office Action also rejects claim 45, alleging that the phrase “including” renders the claim indefinite because it is unclear whether the limitation following the phrase are part of the claimed invention.

Applicants have amended claim 45 to clarify the subject matter claimed. There is no narrowing of scope due to this amendment.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, second paragraph are respectfully requested.

Claim rejections under 35 USC §103(a)

Claims 1, 3, 14, 43-49 are rejected under 35 U.S.C. 103 as being unpatentable over Girasole *et al.*

The Office Action contends that Girasole discloses administering a neutralizing antibody and a monoclonal antibody (mAb) to IL-11 to inhibit osteoclast formation *in vitro*. The Office Action does, however, admit that Girasole fails to disclose a method of administering to any patient such antibodies, and that Girasole fails to teach an increase in osteoblast-mediated bone formation when an IL-11 antibody is administered to patients having a pathological condition in which bone density is decreased. Nevertheless, the Office Action concludes that it would have been *prima facie* obvious, at the time the invention was made, to a skilled artisan to administer such antibodies to such patients, with the expectation that the IL-11 antibodies would decrease osteoclast-mediated bone resorption.

The Office Action contends that “an increase in osteoblast-mediated bone formation... would be inherent to the prior art process disclosed in the reference.” To support its position, the Office Action cites *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990). The Office Action quotes: “it is not necessary in order to establish a *prima facie* case of obviousness [that both a structural similarity between a claimed and prior art compound (or a key component of a composition) be shown and, *omitted from quote*] that there be a suggestion in or expectation from *the prior art* that the claimed [compound or composition, *omitted from quote*] [invention, *added to the quote*] will have the same or a similar utility *as one newly discovered by applicant*,” because “[t]he prior art provided the motivation to make the claimed compositions in the expectation that they would have similar properties.” 919 F.2d at 693 (emphasis original). The Office Action also cites MPEP 2145, paragraph II for case law pertaining to the presence of additional advantages or latent properties not recognized in the prior art. Applicants respectfully disagree.

First of all, the reasoning of the Office Action is based on the mis-characterization that “increase in osteoblast-mediated bone formation” is an additional advantage or latent property not recognized in the prior art. Girasole merely describes an *in vitro* process of inhibiting osteoclast development by IL-11 antibody. It never explicitly or impliedly teaches or suggests the use of IL-11 antibody *in vivo* to treat patients with decreased bone density based on this *in vitro* effect. Therefore, it would be logically inconsistent to conclude that “increase in osteoblast-mediated

bone formation” is an additional advantage or latent property of inhibiting osteoclast function *in vitro*. The Office Action makes the unwarranted quantum leap from disclosing *in vitro* inhibitory effect on osteoclast development to *in vivo* patient treatment. This distinction is by no means trivial, since to recommend treating such patients with such antibodies, one has to be reasonably certain about the other critical part of the equation – the effect of IL-11 antibody on osteoblast function, which the prior art is completely silent. This point is further illustrated below.

The ability to inhibit osteoclast development does not automatically translate into a benefit in treating patients suffering from decrease in bone density, just like the ability of an agent to kill cancer cells does not automatically make that agent an anti-cancer drug. In the latter case, it is obvious that many cytotoxic agents can kill cancer cells *in vitro*, but most of them cannot be used as anti-cancer drugs *in vivo*, since their inherent cytotoxicity also kill normal cells. Only when certain agents *selectively* (or at least *preferentially*) kill cancer cells over normal cells, can they be considered candidates for further drug development. In fact, most anti-mitotic drugs are based on their ability to preferentially kill fast-growing cancer cells over slow-growing or non-proliferating normal cells. At one extreme, an agent that kills cancer cells *and* simultaneously promotes the growth of normal tissue would undoubtedly receive top attention as a drug candidate.

Similarly, there may be numerous agents that are expected to inhibit osteoclast function (such as cytotoxic agents that kill osteoclasts *in vitro*), but that does not automatically make these agents suitable for treating patients with decrease in bone density. In fact, there is no reason to believe that a cytotoxic agent that kills osteoclast would not kill osteoblast (and other cells of the host). There is even less reason to believe that an agent that inhibits osteoclast function by blocking IL-11 signaling would simultaneously have the *opposite* effect (stimulation) on osteoblast function by blocking the same IL-11 signaling. The prior art, including Girasole, never makes such an unexpected discovery, and thus it never teaches or suggests IL-11 antibody as suitable for treating patient with decreased bone density. All Girasole teaches, is that inhibiting IL-11 signaling in osteoclast compromises osteoclast development. This observation is completely silent about the potential effect on osteoblast function, while the claimed invention is partly based on the simultaneous inhibition of osteoclast function *and* stimulation of osteoblast function by inhibiting the same IL-11 signaling pathway in these two different cell types.

Secondly, *In re Dillon* was misapplied since the fact pattern of *Dillon* is distinguishable from that of the instant claimed methods. *Dillon* claimed an improved fuel composition (less soot during combustion) with an alleged novel additive tetra-orthoester. The cited primary prior art disclosed the same fuel composition with a closely related additive, tri-orthoester (for preventing phase separation in the fuel), which tri-orthoester was suggested by several cited secondary prior art as being functionally equivalent to tetra-orthoester, albeit for a different use (as water scavengers in hydraulic fluids). *In re Dillon*, 919 F.2d 688 at 690-691 (Fed. Cir. 1990). In other words, *Dillon* claimed a fuel composition with additive A (useful for utility X), and the prior art disclosed the same fuel composition with additive A' (useful for utility Y), while the prior art also suggested that A and A' were functional equivalents (in yet another utility Z) based on their "close structural and chemical similarity." *Id.* at 691.

Based on prior case law, an earlier panel opinion in the *Dillon* case stated "a *prima facie* case of obviousness is not deemed made unless both (1) the new compound or composition is structurally similar to the reference compound or composition and (2) there is some suggestion or expectation *in the prior art* that the new compound or composition will have the *same or a similar utility as that discovered by the applicant*." *In re Dillon*, 892 F.2d 1554 at 1560 (now withdrawn) (emphasis original). The case was reconsidered *in banc* by a later panel, which overruled the second requirement. See the quote cited above by the Office Action, with the omitted parts restored.

Thus this fact pattern is clearly distinguishable from the instant case. *Dillon* claimed a non-obvious composition based on a newly discovered property of the composition. However, even "[t]he discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957)." See MPEP 2112.02. The claimed invention is yet different from this new-use-for-old-structure type of claim. Applicants claim a method partly based on a known property of a composition with regard to a cell type (as disclosed by the prior art), and a newly discovered unexpected property of the same composition with regard to a different cell type.

A skilled artisan in the *Dillon* case, in view of the prior art, would have motivation to substitute tri-orthoester in the fuel with tetra-orthoester because of the demonstrated structural and chemical similarity between tri- and tetra-orthoesters. Although the prior art there did not suggest

that the resulting fuel composition would have a new property (less soot during combustion), the claimed composition is still *prima facie* obvious, since reduced soot is a mere latent property or undiscovered advantage of the claimed non-obvious fuel composition. In other words, the prior art in *Dillon* teaches and/or suggests all the limitations of the claimed invention, and there is motivation to combine as well as reasonable expectation of success.

However, a skilled artisan, in view of Girasole, would not have used IL-11 antibody to treat patients, since Girasole simply never teaches or suggests so, and the prior art as a whole simply does not provide enough information for reasonable expectation of success in arriving at the claimed invention – a method of using IL-11 to treat patient. The Office Action does not specify that a skilled artisan would be motivated to combine Girasole with other prior art references, if any, to arrive at the claimed method of treating patient with IL-11 antibody.

Pursuant to MPEP 2143, “To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.”

Therefore, none of the three requirement for establishing a *prima facie* case of obviousness is met. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim 50 is rejected under 35 U.S.C. 103 as being unpatentable over Girasole *et al.* (1995) in view of Queen *et al.* (U.S. Pat. No. 5,530,101).

Girasole is discussed above. The Office Action alleges that Green teaches humanization of monoclonal antibodies, thus rendering claim 50 obvious when combined with Girasole.

As argued above, the claimed invention is not obvious in view of Girasole, and Green does not in anyway correct these defects, even assuming a skilled artisan would be motivated to combine Green with Girasole to make humanized antibodies to inhibit osteoclast function.

Accordingly, Applicants submit that all three requirements for establishing a *prima facie* case of obviousness are not met, reconsideration and withdrawal of rejection under 35 U.S.C. 103(a) are respectfully requested.

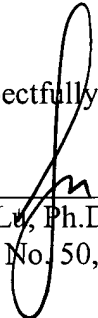
### **CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

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